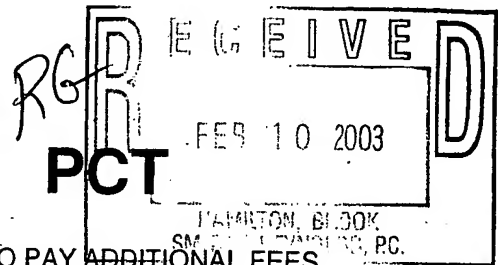


PATENT COOPERATION TREATY

COPY



From the INTERNATIONAL SEARCHING AUTHORITY

To:

HAMILTON, BROOK, SMITH &
REYNOLDS, P.C.
Attn. Collins, Anne J.
530 Virginia Road
P.O. Box 9133
Concord, MA 01742-9133
UNITED STATES OF AMERICA

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FEB 10 2003

INTERNATIONAL
FILING DEPT

INVITATION TO PAY ADDITIONAL FEES

PCT Article 17(3)(a) and Rule 40.1)

DOCKETED

REGISTERED MAIL

Applicant's or agent's file reference

0399.2025005

PAYMENT DUE

within 45 ~~WORK~~ days/days
from the above date of mailing

International application No.

PCT/US 02/ 02392

International filing date
(day/month/year)

28/01/2002

Applicant

WHITEHEAD INSTITUTE FOR BIOMEDICAL RESEARCH

1. This International Searching Authority

- (i) considers that there are 04 (number of) inventions claimed in the international application covered by the claims indicated ~~below~~ on the extra sheet:

FOREIGN DOCKETING
SRU 02-MR-03
ADE 02-MR-03
ADE 17-MR-03

and it considers that the international application does not comply with the requirements of Rules 13.1, 13.2 and 13.3 for the reasons indicated ~~below~~ on the extra sheet:

Update Foreign File Wrapper
Already Docketed

ANNUITY DOCKETING

ANR _____ AND _____

New/Update Annuity (Tax) Card
Already Docketed

Other _____

- (ii) ☒ has carried out a partial international search (see Annex) ☐ will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:

1-11, 15-34, 54-57

- (iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

2. The applicant is hereby invited, within the time limit indicated above, to pay the amount indicated below:

EUR 945.00 x 03 = EUR 2.835.00
Fee per additional invention number of additional inventions total amount of additional fees

Or, _____ x _____ = _____

The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. ☒ Claim(s) Nos. s. PCT/ISA/206 have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority



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Authorized officer

Anna S1lberg

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-11, 15-34, 54-57

A method of enriching an expression library for DNA encoding proteins involved in GLUT4 trafficking at the plasma membrane, a method for identifying a protein involved in insulin stimulated GLUT4 trafficking at the plasma membrane using the forementioned enriched DNA library as well as the proteins identified with said method.

2. Claims: 35-37

Antibody raised against protein L1

3. Claims: 38-44, 47-53

A method for identifying an agent which alters insulin stimulated GLUT4 trafficking at the plasma membrane and a method for altering the insulin stimulated GLUT4 trafficking at the plasma membrane

4. Claims: 45, 46

A method for identifying an agent which binds to a protein comprising a UBX domain

The present application does not meet the requirements of 13(1) PCT because the International Searching Authority is of the opinion that the subject matter of the claims lacks unity and considers that the 4 inventions identified within originally filed claims 1-57 are not so linked as to form a single general inventive concept.

Indeed, the only common concept linking the above subjects is that of the "a protein containing an UBX domain, tentatively called L1". Ladanyi et al. report the identification of the ASPL gene encoding a UBX domain containing protein which is 100 % identical to the claimed L1 protein (figure 8).

Due to the fact that insulin regulated genes, such as Rab4 and VAP-33, are already known in the prior art, (see Vollenweider et al., 1997 and Foster et al., 2000), due to the fact that no other technical feature can be distinguished which in the light of the prior art could be regarded as a special, common identical feature, the ISA is of the opinion that there is no single inventive concept underlying the plurality of different inventions of the present application in the sense of Rule 13.2 PCT.

Consequently, there is a lack of unity, and the different inventions not belonging to a common inventive concept are formulated as the different subjects on the communication pursuant to Article 17(3)(a) PCT.

Therefore, bearing in mind that every one of the inventions

distinguished above (1-4) requires a separate search in the appropriate databases and classified documentation, the ISA considers that the PCT guidelines VII-12 regarding complete search with negligible additional work is not applicable. Thus, only the first invention (claims 1-11, 15-34, 54-57 (all completely)) has been fully searched.

**Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS
OF THE PARTIAL INTERNATIONAL SEARCH**

International Application No

PCT/US 02/02392

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:

see 'Invitation to pay additional fees'

2. This communication is not the international search report which will be established according to Article 18 and Rule 43.

3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.

4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	CARIM-TODD L ET AL: "Identification and characterization of UBXD1, a novel UBX domain-containing gene on human chromosome 19p13, and its mouse ortholog" BIOCHIMICA ET BIOPHYSICA ACTA. GENE STRUCTURE AND EXPRESSION, ELSEVIER, AMSTERDAM, NL, vol. 1517, no. 2, 26 January 2001 (2001-01-26), pages 298-301, XP004248816 ISSN: 0167-4781 figure 1	1-11, 15-34, 54-57
X	LADANYI MARC ET AL: "The der(17)t(X;17)(p11;q25) of human alveolar soft part sarcoma fuses the TFE3 transcription factor gene to ASPL, a novel gene at 17q25." ONCOGENE, vol. 20, no. 1, 2001, pages 48-57, XP009003328 ISSN: 0950-9232	22-24, 32-34
Y	cited in the application page 52, right-hand column, last line -page 53, right-hand column, line 7; figures 6,8	1-11, 15-21, 25-31, 54-57

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS
OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/US 02/02392

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>NAKAYAMA JUN ET AL: "Expression cloning of a human polysialyltransferase that forms the polysialylated neural cell adhesion molecular present in embryonic brain."</p> <p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 92, no. 15, 1995, pages 7031-7035, XP002225896</p> <p>1995</p> <p>ISSN: 0027-8424</p> <p>page 7031, right-hand column, paragraph 2</p> <p>-page 7031, right-hand column, paragraph 4</p> <p>page 4032, right-hand column, paragraphs 2,3</p> <p>---</p>	<p>1-11, 15-21, 25-31, 54-57</p>
X	<p>BARTILSON MAGDALENA ET AL: "Differential fluorescence induction reveals Streptococcus pneumoniae loci regulated by competence stimulatory peptide."</p> <p>MOLECULAR MICROBIOLOGY, vol. 39, no. 1, January 2001 (2001-01), pages 126-135, XP002225897</p> <p>ISSN: 0950-382X</p> <p>page 128, left-hand column, paragraph 2</p> <p>page 132, right-hand column, paragraph 4</p> <p>-page 133, right-hand column, paragraph 1; figures 1-3</p> <p>---</p>	<p>1-11, 15-21, 25-31, 54-57</p>
Y	<p>ORITANI K ET AL: "Identification of stromal cell products that interact with pre-B cells."</p> <p>THE JOURNAL OF CELL BIOLOGY. UNITED STATES AUG 1996, vol. 134, no. 3, August 1996 (1996-08), pages 771-782, XP009001265</p> <p>ISSN: 0021-9525</p> <p>page 772, right-hand column, paragraph 3</p> <p>-page 773, left-hand column, paragraph 3</p> <p>page 773, right-hand column, last paragraph -page 774, left-hand column, paragraph 1</p> <p>---</p> <p style="text-align: center;">-/--</p>	<p>1-11, 15-21, 25-31, 54-57</p>

Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS
OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/US 02/02392

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>SASAKI ET AL: "Expression cloning of a GM3-specific alpha-2,8-sialyltransferase (GD3 synthase)" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 269, no. 22, 3 June 1994 (1994-06-03), pages 15950-15956, XP002084563 ISSN: 0021-9258 page 15951, left-hand column, paragraph 2 -page 15951, left-hand column, paragraph 4 page 15951, right-hand column, last paragraph -page 15952, left-hand column, paragraph 1</p> <p align="center">---</p>	<p>1-11, 15-21, 25-31, 54-57</p>
A	<p>VOLLENWEIDER PETER ET AL: "The small guanosine triphosphate-binding protein Rab4 is involved in insulin-induced GLUT4 translocation and actin filament rearrangement in 3T3-L1 cells." ENDOCRINOLOGY, vol. 138, no. 11, 1997, pages 4941-4949, XP002225898 ISSN: 0013-7227 page 4943, left-hand column, paragraph 2 -page 4943, right-hand column, paragraph 3 page 4945, left-hand column, paragraph 1 page 4946, right-hand column, line 17-22</p> <p align="center">---</p>	<p>1-11, 15-34, 54-57</p>
A	<p>BECKER KARIN ET AL: "Interaction of Fas(Apo-1/CD95) with proteins implicated in the ubiquitination pathway." FEBS LETTERS, vol. 412, no. 1, 1997, pages 102-106, XP002225899 ISSN: 0014-5793 page 104, right-hand column, last paragraph; figures 1,4</p> <p align="center">---</p>	<p>1-11, 15-34, 54-57</p>
A	<p>FOSTER L J ET AL: "A functional role for VAP-33 in insulin-stimulated GLUT4 traffic." TRAFFIC (COPENHAGEN, DENMARK) DENMARK JUN 2000, vol. 1, no. 6, June 2000 (2000-06), pages 512-521, XP002225900 ISSN: 1398-9219 page 514, left-hand column, last paragraph -page 516, right-hand column, paragraph 1; figure 6</p> <p align="center">---</p>	<p>1-11, 15-34, 54-57</p>

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Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS
OF THE PARTIAL INTERNATIONAL SEARCH

International Application No

PCT/US 02/02392

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00 75188 A (GEN HOSPITAL CORP ;WHITEHEAD BIOMEDICAL INST (US); LODISH HARVEY () 14 December 2000 (2000-12-14) claims 1-57 ---	1-11, 15-34, 54-57
A	PATKI VARSHA ET AL: "Insulin action on GLUT4 traffic visualized in single 3T3-L1 adipocytes by using ultra-fast microscopy." MOLECULAR BIOLOGY OF THE CELL, vol. 12, no. 1, January 2001 (2001-01), pages 129-141, XP002225901 ISSN: 1059-1524 page 130, left-hand column, last paragraph -page 130, right-hand column, paragraph 1 page 137, left-hand column, last paragraph -page 139, right-hand column, paragraph 1 ---	1-11, 15-34, 54-57
A	BOGAN JONATHAN S ET AL: "Insulin-responsive compartments containing GLUT4 in 3T3-L1 and CHO cells: Regulation by amino acid concentrations." MOLECULAR AND CELLULAR BIOLOGY, vol. 21, no. 14, July 2001 (2001-07), pages 4785-4806, XP002225902 ISSN: 0270-7306 ---	
*	SIMPSON F ET AL: "GLUT4--at the cross roads between membrane trafficking and signal transduction." TRAFFIC (COPENHAGEN, DENMARK) DENMARK JAN 2001, vol. 2, no. 1, January 2001 (2001-01), pages 2-11, XP002225903 ISSN: 1398-9219 -----	

Patent Family Annex

Information on patent family members

International Application No

PCT/US 02/02392

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0075188	A	14-12-2000	AU 5477500 A	28-12-2000
			EP 1189943 A1	27-03-2002
			WO 0075188 A1	14-12-2000
			US 2002155479 A1	24-10-2002
			US 6303373 B1	16-10-2001
			US 2002052012 A1	02-05-2002

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

Continuation of Box 3.

Claims Nos.: 12-14, 22, 23, 32, 33

Present claims 12-14 relate to a product defined by reference to a desirable characteristic or property, namely, an expression library enriched for DNA encoding a protein involved in GLUT4 trafficking to the plasma membrane.

The claims cover all products having this characteristic or property, whereas the application does not provide support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a search of the claimed scope impossible. Consequently, the search has not been carried out for claims 12-14.

Present claims 22, 23, 32, 33 relate to products defined by reference to a desirable characteristic or property, namely, a protein involved in GLUT4 trafficking to the plasma membrane.

The claims cover all products having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the products by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the products L1 and L2 (page 20, lines 17-28)

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.